backgrounder

Antioxidant Supplements for Health: An Introduction

Antioxidants are substances that may prevent potentially disease-producing cell damage that can result from natural bodily processes and from exposure to certain chemicals. There are a number of different antioxidants found in foods and available as dietary supplements. This fact sheet provides a general overview of antioxidants—with a focus on dietary supplements—and suggests sources for additional information.

Key Points

- People take antioxidant supplements in an effort to improve their health and to prevent various diseases. Examples of commonly used antioxidant supplements include vitamins C and E, selenium, and beta-carotene.
- Although observational studies suggest that eating a diet high in antioxidant-rich vegetables and fruits is associated with a lower risk for many chronic diseases, there is limited evidence to support the use of antioxidant supplements to prevent disease. Additional research, including studies supported by the National Center for Complementary and Alternative Medicine (NCCAM) and other components of the National Institutes of Health (NIH), is under way.
- Tell all of your health care providers about any complementary and alternative practices you use, including antioxidant supplements. Give them a full picture of what you do to manage your health. This will help ensure coordinated and safe care.

About Antioxidants

Oxidation—one of the body's natural chemical processes—can produce "free radicals," which are highly unstable molecules that can damage cells. For example, free radicals are produced when the body breaks down foods for use or storage. They are also produced when the body is exposed to tobacco smoke, radiation, and environmental contaminants. Free radicals can cause damage, known as "oxidative stress," which is thought to play a role in the

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development of many diseases, including Alzheimer's disease, cancer, eye disease, heart disease, Parkinson's disease, and rheumatoid arthritis. In laboratory experiments, antioxidant molecules counter oxidative stress and its associated damage.

The body can produce its own antioxidants and also obtain them from food. Antioxidants are abundant in vegetables and fruits and are also found in grain cereals, teas, legumes, and nuts. Examples of antioxidants include anthocyanins, beta-carotene, catechins, coenzyme Q10, flavonoids, lipoic acid, lutein, lycopene, selenium, and vitamins C and E. Many antioxidants are also available as dietary supplements.

Although antioxidant molecules counter oxidative stress in laboratory experiments, there is some debate as to whether consuming antioxidants—in food or supplement form—actually benefits health. Antioxidant supplements are often synthetic (man-made), but some of these synthetic forms may not have the same effects on the body as antioxidants that occur naturally in foods. In addition, some beneficial properties may be lost when antioxidants are extracted from foods to manufacture supplements. There is also some concern that consuming antioxidants in excessive doses may have negative effects.

Use of Antioxidant Supplements in the United States

In the National Health and Nutrition Examination Survey (NHANES, 1999-2000), over 5,000 of the approximately 10,000 respondents (52 percent), reported taking a dietary supplement in the previous month. Of the 1,900 dietary supplements included in the survey, more than 900 (47 percent) contained an antioxidant: vitamin C, vitamin E, beta-carotene, selenium, flavonoids, or isoflavones. More than 3,000 of the respondents (37 percent) reported taking dietary supplements that contained one of the antioxidants mentioned.

A 2009 study looked at data from NHANES (1999-2000 and 2001-2002) and the U.S. Department of Agriculture Flavonoid Database to estimate the total antioxidant intake (from diet and supplements) of adults in the United States. The researchers calculated the daily intake of vitamin C, vitamin E, carotenes, selenium, and flavonoids. They found that supplements accounted for 54 percent of vitamin C; 64 percent of vitamin E (alpha-tocopherol); 14 percent of carotenes; 11 percent of selenium; and 2 percent of flavonoid intake.

Status of Research on Antioxidant Supplements

There is limited scientific evidence to support the use of antioxidant supplements to prevent disease. Observational studies (which track a group of people without changing their activities or providing special treatments) have shown that a higher intake of antioxidant-rich vegetables and fruits is associated with a reduced risk of certain chronic diseases. It is not clear, however, that the benefits are due to the antioxidants. Although observational studies, as well as laboratory research on the biochemistry of antioxidants, suggest that antioxidant supplements may have beneficial effects, clinical trials (controlled studies in people) have generally found no benefit.

Systematic reviews of the research literature have analyzed the use of antioxidant supplements for preventing cancer, cardiovascular disease, and eye disease, and reducing overall mortality in healthy people and people with various diseases. In general, these reviews have concluded that there is not enough evidence to support the use of antioxidant supplements for these purposes.

Large, long-term studies (randomized, controlled trials) funded primarily by NIH have generally found that antioxidant supplements have no beneficial effects. For example:

- The Physicians Health Study II, which included more than 14,000 healthy male physicians aged 50 or older, found that neither vitamin E nor vitamin C supplements reduced the risk of major cardiovascular events (e.g., heart attack, stroke, or death) or cancer.
- The Selenium and Vitamin E Cancer Prevention Trial (SELECT)—a study of more than 35,000 healthy men aged 50 or older—found that selenium and vitamin E taken alone or together did not prevent prostate cancer. (Two earlier reviews suggested that preliminary evidence for selenium appeared promising). A 2011 updated analysis from this trial concluded that vitamin E supplements significantly increased the incidence of prostate cancer in healthy men. At a median followup of 7 years, the researchers observed that the incidence of prostate cancer was increased by 17 percent in men who received the vitamin E supplement alone compared with those who received placebo. There was no increased incidence of prostate cancer when vitamin E and selenium were taken together.
- The Women's Health Study, which included almost 40,000 healthy women at least 45 years of age, found that overall, vitamin E did not reduce the risk of death, major cardiovascular events (e.g., heart attack, stroke, or death), or cancer. However, it was associated with reduced deaths from cardiovascular causes and also reduced major cardiovascular events in a subgroup of women aged 65 or older.
- The Women's Antioxidant Cardiovascular Study found no beneficial effects of vitamin C, vitamin E, or beta-carotene on cardiovascular events (e.g., heart attack, stroke, or death) in more than 8,000 female health professionals, aged 40 years or older, who were at high risk for cardiovascular disease.

An important exception to this trend is a National Eye Institute study of age-related eye disease, which found that the combination of antioxidants and zinc reduced the risk of developing advanced stages of age-related macular degeneration (AMD) by 25 percent in people who had intermediate AMD or advanced AMD in only one eye. Antioxidant supplements used alone reduced the risk by about 17 percent.

Thus, despite widespread scientific interest and clear plausibility of benefit, the body of evidence for antioxidant supplements has not, to date, demonstrated substantial health benefits. Additional research, some of it aimed at understanding the "disconnect" between findings of laboratory and observational studies and results of clinical trials, is under way.

Safety

Antioxidants in foods are generally considered safe, and studies of antioxidant supplements generally have not reported adverse effects. However, the research does point to some potential concerns; for example, beta-carotene supplements may increase the risk of lung cancer in smokers, and vitamin E supplements may increase the risk of bleeding in certain individuals. More research is needed to better understand the safety aspects of dietary supplementation. For more information about dietary supplements, see the NCCAM fact sheets Using Dietary Supplements Wisely and Are You Considering CAM?

If You Are Thinking About Using Antioxidant Supplements

- Do not use antioxidant supplements as a replacement for a healthful diet or conventional medical care, or as a reason to postpone seeing a doctor about a medical problem.
- Consult your health care provider before deciding to use antioxidant supplements.
- Look for published research studies on antioxidant supplements for the health condition that interests you.
- Tell all of your health care providers about any complementary and alternative practices
 you use. Give them a full picture of what you do to manage your health. This will help
 ensure coordinated and safe care. For tips about talking with your health care providers
 about complementary and alternative medicine (CAM), see NCCAM's Time to Talk
 campaign at nccam.nih.gov/timetotalk/.

NCCAM-Funded Research

Because antioxidants are widely used, and because there is laboratory and observational evidence of potential health benefits, antioxidants are the subject of extensive research across NIH, including recent NCCAM-sponsored studies that have been investigating:

- Three antioxidant regimens—**Ginkgo biloba, alpha-lipoic acid/essential fatty acids,** and **vitamin E/selenium**—as potential treatments for multiple sclerosis
- **Lipoic acid**, an antioxidant used in the treatment of diabetic neuropathy, to improve blood vessel reactivity and decrease oxidative stress in people with high cholesterol
- The safety of the vitamin E supplement **gamma-tocopherol** in healthy people and those with asthma and allergies
- The combination of **vitamins E** and **C** to enhance airway antioxidant levels in people with allergic asthma and reduce the incidence of preeclampsia among pregnant women with chronic hypertension or a history of preeclampsia/eclampsia
- Alpha-lipoic acid and fish oil to slow the progression of Alzheimer's disease

- Whether **alpha-tocopherol** (vitamin E) supplementation affects the progression of carotid atherosclerosis (narrowing or hardening of the carotid artery) in patients with coronary artery disease
- The safety and efficacy of **vitamin E** in slowing the rate of cognitive and functional decline in older persons with Down syndrome.
- NCCAM also funds two research centers that are studying the effects of antioxidants on aging, amyotrophic lateral sclerosis (ALS, commonly known as Lou Gehrig's disease), asthma, and cardiovascular diseases.

Other NIH studies on antioxidants have been investigating:

- The effects of **vitamin C** on the lung development and function of babies born to women who smoke during pregnancy
- Whether an antioxidant drug (**n-acetylcysteine**) taken orally will improve glucose tolerance and insulin secretion in type 2 diabetic subjects
- The safety and effectiveness of **coenzyme Q10** (combined with **vitamin E**) to slow the progression of Parkinson's disease
- The side effects and best dose of high-selenium Brassica juncea (mustard plant) and capecitabine (a cancer drug) given together with irinotecan (a cancer drug) as a treatment for patients with advanced cancer
- Whether antioxidants (**beta-carotene**, **vitamin C**, and **vitamin E**) combined with magnesium can prevent noise-induced hearing loss.

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For More Information

NCCAM Clearinghouse

The NCCAM Clearinghouse provides information on CAM and NCCAM, including publications and searches of Federal databases of scientific and medical literature. The Clearinghouse does

not provide medical advice, treatment recommendations, or referrals to practitioners.

Toll-free in the U.S.: 1-888-644-6226

TTY (for deaf and hard-of-hearing callers): 1-866-464-3615

Web site: nccam.nih.gov

E-mail: info@nccam.nih.gov

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Web site: www.ncbi.nlm.nih.gov/sites/entrez CAM on PubMed®: nccam.nih.gov/research/camonpubmed/

ClinicalTrials.gov

ClinicalTrials.gov is a database of information on federally and privately supported clinical trials (research studies in people) for a wide range of diseases and conditions. It is sponsored by the National Institutes of Health and the U.S. Food and Drug Administration.

Web site: www.clinicaltrials.gov

Research Portfolio Online Reporting Tool (RePORT)

RePORT is a database of information on federally funded scientific and medical research projects being conducted at research institutions.

Web site: www.projectreporter.nih.gov/reporter.cfm

NIH National Library of Medicine's MedlinePlus

To provide resources that help answer health questions, MedlinePlus brings together authoritative information from the National Institutes of Health as well as other Government agencies and health-related organizations.

Web site: www.medlineplus.gov

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